



Analysis and Modeling of Frequency-Specific Habituation of the Goldfish Vestibulo-Ocular Reflex

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Abstract. Modification of the vestibulo-ocular reflex (VOR) by vestibular habituation is an important paradigm in the study of neural plasticity. The VOR is responsible for rotating the eyes to maintain the direction of gaze during head rotation. The response of the VOR to sinusoidal rotation is quantified by its gain (eye rotational velocity/head rotational velocity) and phase difference (eye velocity phase—inverted head velocity phase). The frequency response of the VOR in naïve animals has been previously modeled as a high-pass filter (HPF). A HPF passes signals above its corner frequency with gain 1 and phase 0 but decreases gain and increases phase lead (positive phase difference) as signal frequency decreases below its corner frequency. Modification of the VOR by habituation occurs after prolonged low-frequency rotation in the dark. Habituation causes a reduction in low-frequency VOR gain and has been simulated by increasing the corner frequency of the HPF model. This decreases gain not only at the habituating frequency but further decreases gain at all frequencies below the new corner frequency. It also causes phase lead to increase at all frequencies below the new corner frequency (up to some asymptotic value). We show that habituation of the goldfish VOR is not a broad frequency phenomena but is frequency specific. A decrease in VOR gain is produced primarily at the habituating frequency, and there is an increase in phase lead at nearby higher frequencies and a decrease in phase lead at nearby lower frequencies (phase crossover). Both the phase crossover and the frequency specific gain decrease make it impossible to simulate habituation of the VOR simply by increasing the corner frequency of the HPF model. The simplest way to simulate our data is to subtract the output of a band-pass filter (BPF) from the output of the HPF model of the naïve VOR. A BPF passes signals over a limited frequency range only. A BPF decreases gain and imparts a phase lag and lead, respectively, as frequency increases and decreases outside this range. Our model produces both the specific decrease in gain at the habituating frequency, and the phase crossover centered on the frequency of habituation. Our results suggest that VOR habituation may be similar to VOR adaptation (in which VOR modification is produced by visual-vestibular mismatch) in that both are frequency-specific phenomena.

Keywords: habituation, adaptation, vestibulo-ocular reflex, goldfish, linear systems

Introduction

To maintain the direction of gaze during voluntary or involuntary head rotations, eyes must make compensatory rotations opposite to head rotations. These eye rotations are mediated primarily by the vestibulo-ocular reflex (VOR) at higher frequencies. If not for these compensatory eye movements by the VOR, vision would be blurred during higher-frequency head movement, making it impossible to move and see simultaneously. Although it works in conjunction with the visual system, the VOR does not rely on visual input to make compensatory eye movements. The basic VOR pathway is a relatively simple three-neuron arc (Baker et al., 1981). Head rotational velocity is transduced by the semicircular canal receptors. Semicircular canal afferent neurons send a head velocity signal to vestibular nucleus neurons (VN). The VN in turn project to the extraocular motoneurons, which produce eye rotation.

Due primarily to dynamic limitations of the semicircular canals, the VOR works best at higher frequencies. The VOR response is close to ideal for head rotational frequencies above about 0.1 Hz, with a gain (eye rotational velocity/head rotational velocity) of unity and no phase difference (eye velocity phase—inverted head velocity phase). This ensures that the image projected on the retina doesn't move during head rotations at higher frequencies. At lower frequencies, the VOR exhibits a phase lead (positive phase difference) and a decrease in gain. This response can be modeled as a linear high-pass filter (HPF), which has similar frequency response characteristics (Wilson and Melvill Jones, 1985; Blair and Gavin, 1979; Jäger and Henn, 1981a; Baloh et al., 1982; Weissenstein et al., 1996).

The VOR is highly plastic, probably so that it can maintain its critical functionality despite changes to the animal such as growth, age-related deterioration of the vestibular or oculomotor periphery, or injury to vestibular afferents or vestibular nucleus neurons. The VOR shows various forms of plasticity, which include vestibular compensation, adaptation, and habituation. Vestibular compensation is the plastic process by which an animal can at least partially recover normal VOR function following the lesioning of one of the pair of vestibular receptors (for review, see Smith and Curthoys, 1989). Vestibular adaptation involves plastic changes in the VOR brought about through visual/vestibular mismatch (see below). Vestibular compensation (Ratnam and Anastasio, 1995;

Weissenstein et al., 1996) and adaptation (Schairer and Bennett, 1986; Pastor et al., 1992) results show that the VOR of goldfish is more plastic than that of other animals studied.

The VOR will habituate to repeated or prolonged low-frequency rotations delivered in darkness (Dodge, 1923). Habituation produces an attenuation in both the strength and the duration of the VOR response (for review, see Schmid and Jeannerod, 1985). Repeated step accelerations result in a decrease in the amplitude and duration of the VOR step response. Prolonged rotations at lower frequencies can cause a decrease in VOR gain (Buettner et al., 1981; Jäger and Henn, 1981a, 1981b; Baloh et al., 1982; Dow and Anastasio, 1996, 1997, 1998a). This decrease in VOR response can last for days or weeks in cat (Henriksson et al., 1961; Collins and Updegraff, 1965; Jeannerod et al., 1976; Clément et al., 1981), dog (Collins and Updegraff, 1965), and goldfish (Dow and Anastasio, 1998a) and for months in monkey (Jäger and Henn, 1981a) and human (Collins, 1964; Jäger and Henn, 1981b). Repeated or prolonged rotations at higher frequencies (>0.1 Hz), produce little or no change in the gain of the VOR (Ito et al., 1974; Kleinschmidt and Collewyn, 1975; Jäger and Henn, 1981a; Dow and Anastasio, 1996, 1997).

Both the decrease in low-frequency gain observed during habituation to low-frequency rotation and the reduction in response amplitude following repeated step accelerations have been simulated as a reduction in the dominant time constant of the HPF model of the VOR (Blair and Gavin, 1979; Buettner et al., 1981; Jäger and Henn, 1981a; Baloh et al., 1982). The linear, HPF model of the VOR—

$$\frac{\dot{E}(s)}{\dot{H}(s)} = g_v \frac{s\tau_v}{s\tau_v + 1} \quad (1)$$

—relates eye velocity (\dot{E}) to head velocity (\dot{H}), where g_v and τ_v are the VOR gain and time constants, respectively, and s is the Laplace variable ($s = j\omega$ where $j^2 = -1$ and ω is the frequency in radians/sec). The time constant (τ) specifies the corner frequency of a high- or low-pass filter:

$$\text{Corner frequency (Hz)} = \frac{1}{2\pi\tau}. \quad (2)$$

A first-order HPF (Fig. 1A and B) passes signals with no change to gain or phase at frequencies above its corner frequency but decreases gain and produces a phase lead that asymptotes at 90 deg at frequencies below the

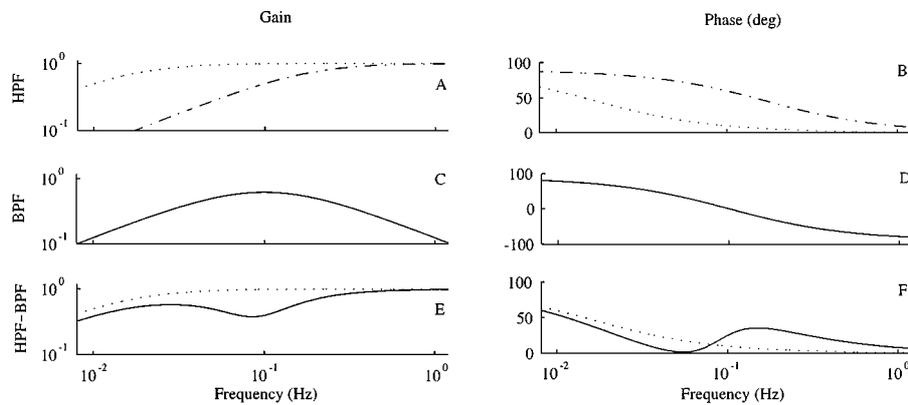


Figure 1. Prototypical frequency responses from the HPF-BPF model (Fig. 5). A, B: The naïve VOR frequency response (dotted lines) was modeled as a first-order HPF. For comparison, modeling habituation by decreasing the time constant of a that HPF by an order of magnitude is shown by the dot-dashed lines. C, D: The frequency response of a BPF. E, F: The difference (HPF-BPF, solid line) shows the gain dip and phase crossover not seen in the naïve HPF (dotted lines). The gain constant of each transfer function is identical ($g_v = g_b = 1$). Values of other parameters are $\tau_v = 10.4$ s, $cf = 0.1$ Hz, and $\lambda = 0.1$ ($\tau_l = 1.26$ s and $\tau_h = 2.00$ s). The subtraction causes a decrease in gain centered on the cf and also causes a decrease in phase lead at nearby lower frequencies and an increase in phase lead at nearby higher frequencies. The resultant dip in gain is shifted to lower frequency, as is the phase crossover, due to the phase lead and gain decrement of the HPF.

corner frequency. If decreasing the time constant of the HPF is a valid model of habituation, a set of data from habituated animals should be indistinguishable from a set of data from naïve animals that has been shifted by a constant frequency.

Decreasing the time constant of a HPF increases its corner frequency (Fig. 1A and B). This causes a reduction in gain for all frequencies below the new corner frequency, including a further reduction in the gain for all frequencies below the old corner frequency. Increasing the corner frequency can simulate habituation by decreasing gain at the habituating frequency. It also causes an increase in phase lead for all frequencies below the new corner frequency including the habituating frequency (up to an asymptote of 90 deg). An increase in VOR phase lead at the habituating frequency has been observed in some studies (Jäger and Henn, 1981a, 1981b; Baloh et al., 1982), but not in others (Buettner et al., 1981; Jäger and Henn, 1981a). A lack of a consistently observed increase in the phase lead at the habituating frequency would suggest that a HPF model of VOR habituation may be incorrect. Systematic studies of the frequency response of the VOR following prolonged rotation at specific frequencies have not been performed. The purpose of this study is to do these experiments.

Habituation of the goldfish VOR to low-frequency rotation is associated with static and dynamic nonlinear behavior. Nonlinear aspects of the VOR that have been

observed in goldfish include violation of superposition, abrupt decreases in gain during habituation, asymmetric habituation, magnitude dependent responses, and periodic alternating nystagmus (see Discussion for relevant details). The nonlinear behavior of the VOR associated with habituation has been described in previous articles (Dow and Anastasio, 1996, 1997, 1998a). This article focuses on changes in VOR gain and phase in habituated goldfish that can be described using linear systems concepts.

Vestibular adaptation has been studied more extensively than vestibular habituation as a form of VOR plasticity. Adaptation occurs when the input to the visual system is altered such that it is no longer consistent with the rotation of the animal in its environment. Changes in the vestibular system following adaptation are evident during rotation in the dark. Adaptation causes an appropriate modification of VOR gain (either increase or decrease) primarily at the frequency of rotation to reduce the dysmetria between the two systems (for review, see Melvill Jones, 1985; Cohen et al., 1992; Torte et al., 1994). When VOR gain is decreased, there is a decrease in phase lead at nearby lower frequencies and an increase in phase lead at nearby higher frequencies relative to the frequency of rotation (Godaux et al., 1983; Lisberger et al., 1983; Schairer and Bennett, 1986; Raymond and Lisberger, 1996). The phase changes are reversed if the VOR gain is increased. These changes in phase have been described

as a phase crossover (Lisberger et al., 1983). The frequency specific gain changes as well as the phase crossover cannot be described adequately with a HPF model of the VOR. Miles et al. (1985) proposed a model to explain the changes in gain and the phase crossover observed during frequency-selective adaptation. Their model consists of multiple, parallel band-pass filters in the brainstem that are each tuned for a slightly different frequency (see Discussion).

It is possible that vestibular habituation, like vestibular adaptation, may also be frequency specific. If so, an animal experiencing prolonged single-frequency rotation in the dark might produce a decrease in VOR gain primarily at the habituation frequency as well as a crossover in phase. We will show that this is indeed the case for habituation of the goldfish VOR. The data suggest that habituation of the goldfish VOR cannot be modeled by simply decreasing the value of the time constant (that is, increasing the corner frequency) of the HPF model of the VOR. This manipulation of the model produces changes in gain and phase over broad ranges of frequency that are inconsistent with the frequency-specific effects we observe. We will propose that the simplest way to model the frequency-specific changes we observe during habituation is by subtracting the output of a band-pass filter from that of the HPF model of the VOR. In that they are both similarly frequency specific, our experimental and modeling results suggest that vestibular habituation is more similar to vestibular adaptation than previously supposed.

Methods

Changes in the VOR frequency response due to habituation by prolonged single-frequency rotation were studied in comet goldfish (*carassius auratus*). Each goldfish was intact and experimentally naïve (that is, had no previous exposure to experimental rotation). Goldfish were 10 to 15 cm in length. Each goldfish was wrapped in cloth and restrained horizontally underwater, using contoured body supports positioned caudal to the gills, in a 10 l cylindrical tank. The head was immobilized by tying the mouth around a rigid tube. Aquarium water was continually recirculated through the tube for respiration. To measure eye movements, a small coil of insulated wire (5.3 mm external coil diameter) was attached to the tough outer covering of the left eye using ophthalmic suture. This tissue is tough and insensitive and general anesthesia was not necessary. Once the eye coil was in place, rotations were

begun after approximately 10 min. A search coil system (Rommel Labs, Ashland, MA) was used to transduce eye position (Robinson, 1963; Rommel, 1984). Immediately following each experiment the system was calibrated to 0.1 deg at seven angles that covered the range of eye movement (± 30 deg).

The tank was mounted on the horizontally oriented platform of a servo-driven rotating device. Both the tank and the fish's head were centered on the vertical axis of rotation. This minimized translational acceleration of the head during rotation, ensuring that rotation stimulated only the semicircular canals and not the otoliths. To ensure that no visual input was available to the animal during experiments, the tank was shrouded in two layers of black mylar and the room lights were extinguished. The eye position and rotator tachometer (head velocity) signals were digitized with a 12 bit AD converter. Digitization rates were 50 or 300 Hz for rotational frequencies below or equal to 1 Hz, respectively. Signals were digitized after antialias filtering (8-pole Butterworth) at half the sampling rate.

The frequency response of the VOR over the range extending from 0.01 to 1.0 Hz was measured in 30 goldfish after 1 h of habituation at a specific frequency within the range. To measure the frequency response, VOR gain and phase were determined for rotations at each of the following seven single frequencies in order: 1.0, 0.5, 0.3, 0.1, 0.05, 0.03, and 0.01 Hz. Rotations lasted 1 min at 1.0 Hz, 2 min at 0.5, 0.3, and 0.1 Hz, 4 min at 0.05 Hz, 6 min at 0.03 Hz, and 20 min at 0.01 Hz. All stimuli had peak rotational velocities of 60 deg/s, and each rotation was gradually ramped up to peak velocity in 10 to 15 s to minimize transients.

The naïve frequency response was measured in 12 goldfish. The act of measuring the VOR response to lower frequencies of rotation changes the properties of the VOR. Goldfish can begin to habituate to 0.01 Hz rotation during the first cycle of rotation (Dow and Anastasio, 1998a), so the animal must be considered at least partially habituated at 0.01 Hz after measuring the naïve frequency response. Therefore, the naïve frequency response was only measured in goldfish that were subsequently habituated to 0.01 Hz rotations. Accordingly, in animals that were to be habituated at other frequencies, the naïve frequency response was not measured. In all cases, the frequency response was tested again following habituation. As stated above, all goldfish began in this study naïve.

Eye position data were digitally differentiated to compute eye velocity, and fast-phases were removed

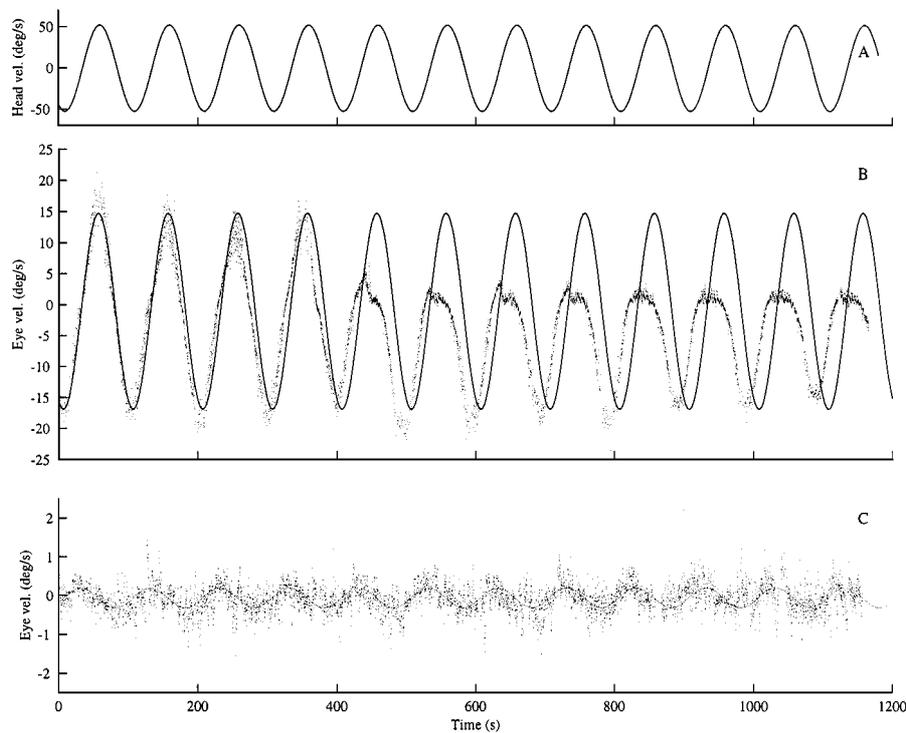


Figure 2. Time series illustrating the habituating and habituated VOR at 0.01 Hz. Inverted head velocity during 0.01 Hz rotations (A) is compared to the VOR eye velocity of naïve habituating (B) and habituated (C) goldfish. To show changes in VOR gain and phase the sinusoids shown in (B) and (C) were fit by minimizing the least-squares error for the first cycle of the data only and then propagated with the same parameters to the end of the graph. Phase lead increases during the first 20 min of 0.01 Hz rotation (B) and becomes pronounced during the fifth cycle. The VOR eye velocity waveform also becomes distorted during the fifth cycle (nasal rectification), though nonsinusoidal portions are observable on the second cycle. C: Habituation becomes severe after 40 min of rotation. The response is attenuated but clearly sinusoidal. The vertical scales for (B) and (C) are different. Nasally and temporally directed eye rotational velocities are given positive and negative values, respectively.

automatically (Fig. 2). The slow-phase eye velocity amplitude and phase were estimated by fitting least-square sinusoids to the remaining slow-phase eye-velocity data. Head-velocity amplitude and phase were measured by fitting least-squares sinusoids to the rotator tachometer data. VOR gain was calculated by dividing peak slow-phase eye-velocity amplitude by peak head-velocity amplitude. The head-velocity record was inverted to bring head- and eye-velocity phases into the same range to facilitate comparisons. VOR phase difference was calculated by subtracting the inverted head-velocity phase from the eye-velocity phase. During prolonged rotation at midfrequencies (0.03 to 0.17 Hz), the goldfish VOR can exhibit a very-low-frequency oscillation (period >2 min) superimposed on the normal response that is called *periodic alternating nystagmus* (PAN) (Dow and Anastasio, 1997, 1998b). The slowly changing baseline due to PAN, when present, could produce errors in VOR gain and

phase estimates. Therefore, VOR gain and phase were made only from short duration records. Normally, 100 s of data were fit at 0.01, 0.03, and 0.05 Hz, 60 s at 0.1 and 0.3 Hz, 40 s at 0.5 Hz, and 10 s at 1.0 Hz. Habituation can also produce nonlinearities such as asymmetries in the VOR response, especially at the lower frequencies (0.01 to 0.05 Hz) (Dow and Anastasio, 1996, 1998a). To make more accurate estimates of VOR gain and phase, nonlinear portions of the data were removed for fitting purposes, as we have done in previous work (e.g., Dow and Anastasio, 1998a, Fig. 1).

Due to the presence of a few extreme values, the median rather than the mean was used as a measure of central tendency, and the first and third quartiles provided the associated measures of variability. Significance was tested nonparametrically with a two-tail Mann-Whitney U test. Changes in gain and phase in each set of habituated goldfish ($n = 12$ or $n = 3$) were

compared directly to the naïve population ($n = 12$). Data were analyzed and modeled using MATLAB (The Mathworks, Inc.). This article focuses on the linear aspects of these data. The nonlinear aspects have been described in previous articles (Dow and Anastasio, 1996, 1997, 1998a).

Results

Experimental

To characterize the frequency response of the naïve goldfish VOR, we estimated the gain and phase of naïve VOR responses to sinusoidal rotation at seven single frequencies. This involved fitting least-squares sinusoids using an optimization routine (see Methods). The VOR response to 0.01 Hz rotation is illustrated in Fig. 2B. At low frequencies where habituation can alter the VOR response (as in Fig. 2B at 0.01 Hz), the naïve response is measured from the first few cycles (see below and Methods). The average VOR frequency response from 12 naïve goldfish, over the frequency range extending from 0.01 to 1.0 Hz, is shown in Fig. 3A and B. Previously, researchers have shown that the naïve goldfish VOR frequency response has a relatively constant gain over two decades of frequency with some modest phase lead at lower frequencies (Pastor et al., 1992; Weissenstein et al., 1996). We find similar frequency response characteristics over the range tested (see Fig. 3A and B). The naïve goldfish VOR has a slight phase lead at lower frequencies, with phase lead near 0 at higher frequencies. However, the phase lead data for 0.01 Hz rotations in naïve goldfish were not symmetrically distributed. Instead, phase leads were clustered near 0 with a tail toward increased phase leads (Fig. 3B). The VOR of the naïve goldfish did not normally exhibit a phase lag at any of the frequencies tested.

Prolonged rotation at lower frequencies (≤ 0.1 Hz) will produce habituation of the VOR, which is characterized primarily as a decrease in gain, but phase changes can also occur. When naïve goldfish were habituated at 0.01 Hz, phase lead did not continuously increase during sinusoidal rotation as has been reported in human (Jäger and Henn, 1981b). Instead, phase lead increased initially and then decreased. To illustrate the changes in VOR gain and phase during the initial period of habituation at 0.01 Hz, the sinusoid that was fit to the first cycle of slow-phase eye velocity in Fig. 1B has

been propagated for the remainder of the record. The figure shows that the naïve VOR decreases in gain and increases in phase lead as rotation continues during the first 20 min of the habituation period. It also illustrates nonstationarities and nonlinearities, especially asymmetries, that are characteristic of the habituating VOR (Dow and Anastasio, 1998a) (see Introduction). The VOR response to 0.01 Hz rotation starting after 40 min of habituation at this frequency is shown in Fig. 2C. The high-frequency noise originates from natural variability in goldfish slow-phase eye position, and transducer and digitization noise, which is magnified by differentiation to eye velocity and made apparent by the high magnification of the record (Fig. 2C). Again, the fit to the first cycle of slow-phase eye velocity is propagated for the rest of the record. The habituated VOR response is greatly attenuated but still sinusoidal. Gain and phase can be well estimated even when habituation has greatly reduced gain.

To illustrate the relationship between VOR gain and phase during habituation to 0.01 Hz rotation (e.g., Fig. 2), gain is plotted against phase in four typical goldfish in Fig. 4. In all 12 goldfish rotated at 0.01 Hz for 1 h, there was a concurrent decrease in VOR gain and an increase in phase lead during the first 10 to 20 min. Phase lead peaked after 20 to 30 min and then decreased as VOR gain continued to decrease. The final phase lead after 1 h of 0.01 Hz rotation was quite variable (see also error bars in Fig. 3D). Small, variable phase changes were often associated with the habituation process at other frequencies, but a systematic increase followed by a decrease in phase lead (as shown in Fig. 4) was not observed at any other frequency during 1 h of continuous rotation (see Discussion).

The purpose of this work is to develop and compare linear system descriptors of the goldfish VOR before and after habituation at single frequencies. To do this, VOR gain and phase were estimated at single frequencies over a frequency spectrum. The single frequencies were tested in the following order: 1.0, 0.5, 0.3, 0.1, 0.05, 0.03, and 0.01 Hz. The frequency response was measured in 12 naïve goldfish. These same 12 goldfish were then habituated at 0.01 Hz by 1 h of rotation at that frequency. Additionally, 18 naïve goldfish were habituated to one of the six other frequencies (three goldfish for each of the other single frequencies in the spectrum) by rotation at that frequency for 1 hour. The naïve VOR frequency response was not first tested in goldfish that were habituated at frequencies other than 0.01 Hz because testing the frequency response would

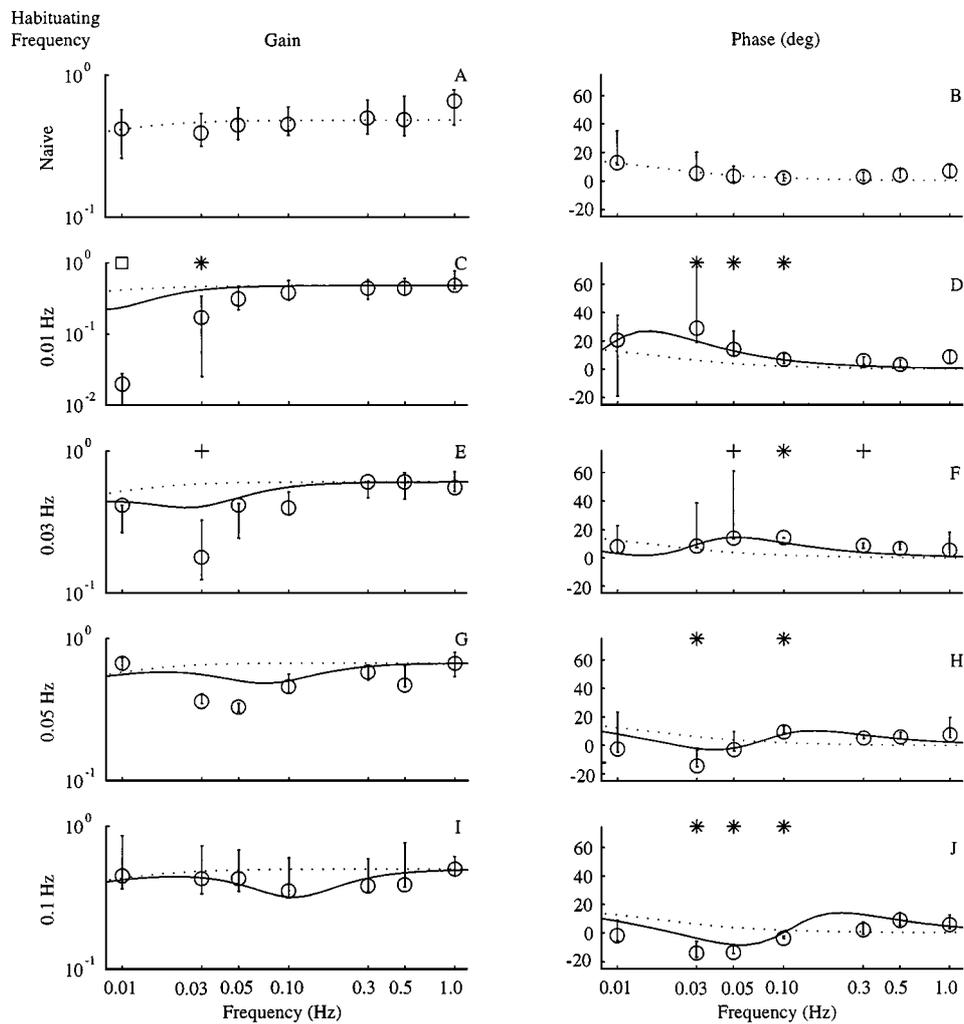


Figure 3. VOR gain and phase from naïve goldfish and goldfish habituated to single frequency sinusoidal rotations. For A–D, where $n = 12$, circles show medians and error bars show first and third quartiles. For E–J, where $n = 3$, circles show middle values and error bars show the high and low values, which are equivalent to the median and first and third quartiles, respectively. Dotted lines show the fit of the arbitrary-order HPF transfer function to the naïve response in all plots. Solid lines (C–J) show the fit of the HPF-BPF model. In fitting the HPF-BPF, the gain of the HPF was adjusted to match the highest gain value in the habituated data and fixed at that value. The other HPF parameters were unchanged from naïve values and also fixed. Only the central frequency and the width of the BPF were iterated by the optimization routine in fitting the HPF-BPF model to the data. Data from habituated goldfish that were statistically different from naïve values are indicated by a \square ($p < 0.0001$), a $*$ ($p < 0.01$), or a $+$ ($p < 0.05$) above the data. All vertical scales are the same except for C, which is compressed to show the large decrease in gain at 0.01 Hz. Phase leads are given positive values. Parameters used for the BPF component of the model are shown in Table 1.

have exposed them to 0.01 Hz rotations and they would not have been naïve at the start of the habituation period. After single-frequency habituation, the habituated VOR gain and phase were measured at all seven frequencies in the spectrum.

One hour of rotation at single frequencies could produce decreases in VOR gain not only at the habituating frequency but at nearby frequencies as well. The amount and extent of VOR gain decrease was greater

for lower than for higher habituating frequencies. One hour of rotation produced consistent decreases in VOR gain at the habituating frequency for frequencies in the lower half of the spectrum (0.01 to 0.1 Hz). The VOR frequency response of naïve goldfish, and of goldfish habituated at single frequencies in the range from 0.01 to 0.1 Hz, are compared in Fig. 3. One hour of rotation at single frequencies in the upper half of the spectrum (0.3 to 1.0 Hz) did not decrease VOR gain at the

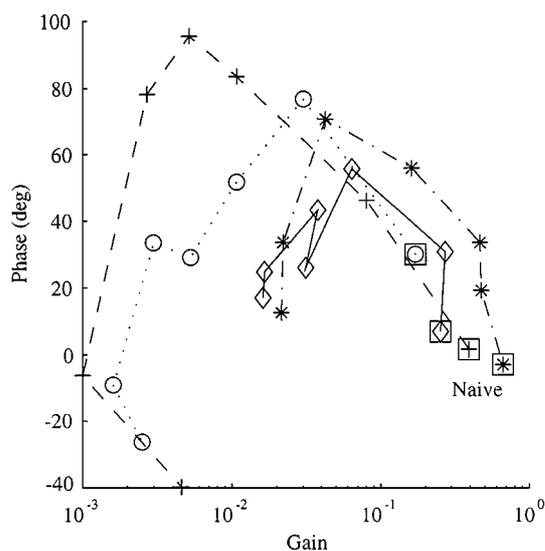


Figure 4. VOR gain plotted against phase, measured every 10 min in four typical goldfish during 1 h of habituation at 0.01 Hz. Naïve data are plotted inside a square and have relatively high gains with phases close to 0. As rotation and habituation continues, phase lead increases as gain decreases. Between 20 and 40 min of 0.01 Hz rotation, phase lead peaks and then decreases while gain continues to decrease. Phase lead can remain positive or can become a phase lag.

habituating frequency nor at any other frequencies in the spectrum. VOR frequency responses for goldfish habituated at these frequencies are not shown.

One hour of rotation at either of the two lowest frequencies caused statistically significant changes in VOR gain. For the lower frequencies of habituation (0.01 to 0.1 Hz) the largest decrease in VOR gain was always at the habituating frequency (Fig. 3C,E,G and I). Gain also decreased at frequencies tested near the habituating frequency. This results in a “dip” in the gain plots at and near the habituating frequency. The decrease in gain at 0.01 Hz was statistically significant relative to naïve after 1 h of rotation at this frequency ($p < 0.0001$). In addition, goldfish habituated at 0.01 Hz also showed a significant decrease in gain at 0.03 Hz ($p < 0.05$). Gain for goldfish habituated at 0.03 Hz also decreased significantly at the habituating frequency compared with naïve goldfish ($p < 0.05$). Gain decreased in each goldfish at the habituating frequency when habituated at 0.05 or 0.1 Hz, but the decreases were not statistically significant when compared with naïve goldfish ($p > 0.05$). There were no statistically significant changes in gain for goldfish rotated for 1 h at higher frequencies (0.3 to 1.0 Hz).

One hour of rotation also caused statistically significant changes in VOR phase. For the lower frequencies of habituation (0.01 to 0.1 Hz) a phase crossover was observed. The phase crossover was centered on the habituating frequency and resulted in a decrease in phase lead (usually resulting in a small phase lag) at nearby lower frequencies and an increase in phase lead at nearby higher frequencies. For goldfish habituated at 0.01 Hz, phase lead did not increase significantly at the habituating frequency ($p > 0.05$). However, there were statistically significant ($p < 0.01$) increases in VOR phase lead compared with naïve goldfish at 0.03, 0.05, and 0.1 Hz (Fig. 3D). For goldfish habituated at 0.03 Hz (Fig. 3F), there were statistically significant increases in phase at 0.05 Hz ($p < 0.05$), 0.1 Hz ($p < 0.01$), and 0.3 Hz ($p < 0.05$). For goldfish habituated at 0.05 Hz (Fig. 3H), both the decrease in phase lead at 0.03 Hz and the increase in phase lead at 0.1 Hz were statistically significant ($p < 0.01$). For goldfish habituated at 0.1 Hz (Fig. 3J), there was a statistically significant decrease in phase lead ($p < 0.01$) at 0.03, 0.05, and 0.1 Hz. There were no significant changes in phase for goldfish rotated for 1 h at higher frequencies (0.3 to 1.0 Hz).

For goldfish habituated at frequencies between 0.01 and 0.1 Hz, gain was always lowest at the habituating frequency. Gain could also decrease at nearby lower and higher frequencies but did not decrease at all lower frequencies, as would be predicted from the HPF model of VOR habituation. Phase lead decreased and increased at nearby frequencies below and above the habituating frequency, respectively. Phase lead did not increase (up to an asymptote) at all frequencies lower than the habituating frequency, as would have been predicted from the HPF model. The frequency-specific effects of VOR habituation described above, which have not been reported previously, necessitate a change in the HPF model of this process. We propose a better model below. Our frequency-specific VOR habituation results are qualitatively similar to those reported in VOR adaptation studies where there is a dip in gain and a phase crossover centered on a specific frequency. The similarities (and differences) between VOR habituation and adaptation will be expanded further in the Discussion.

Model

To provide a linear system descriptor of the naïve goldfish VOR (Fig. 3A, B) a linear, arbitrary-order

HPF of the form

$$\frac{\dot{E}(s)}{\dot{H}(s)} = g_v \left(\frac{s\tau_v}{s\tau_v + 1} \right)^{k_v} \quad (3)$$

was fit to the naïve goldfish frequency-response data. An arbitrary-order (as opposed to a fixed-order) HPF provides an extra degree of freedom that is needed to model the frequency response of the naïve goldfish VOR (Weissenstein et al., 1996). Any HPF passes signals above its corner frequency (2) with log gain 0 and phase 0. For an arbitrary-order HPF, log gain falls with a slope of k_v , and phase lead rises to an asymptote of $k_v \cdot 90$ deg, as the log of signal frequency decreases below the corner frequency. For the naïve goldfish VOR, log gain falls at a rate less than 1, and phase lead rises to an asymptote of less than 90 deg, as log frequency decreases below the corner frequency. Therefore, $0 < k_v < 1$ for the HPF model of the VOR in naïve goldfish (Weissenstein et al., 1996). It should be noted that gain and phase do not change abruptly at the corner frequency, as its common name might imply. Rather, gain and phase change smoothly with frequency as illustrated for an order-1 HPF ($k_v = 1$) in Fig. 1A and B.

In order to fit each HPF (3) the following error function was minimized:

$$\text{Error} = \sum_{i=1}^7 (\log_{10}(\hat{g}_i) - \log_{10}(g_i))^2 + (\hat{p}_i - p_i)^2, \quad (4)$$

where i is one of the seven frequencies in the spectrum, and \hat{g}_i is the estimated gain, g_i is the actual gain, \hat{p}_i is the estimated phase in deg, and p_i is the actual phase. Using \log_{10} gain rather than gain in the error calculations gave the gain values more comparable weightings to phase over the frequency spectrum and resulted in better fits. Fitting log gain and phase, rather than the real and imaginary components of the transfer function evaluated at each frequency, allowed gain at certain frequencies to be removed from certain fits while phase at those frequencies remained (see below and Discussion). The optimization procedure varied the parameters g_v , τ_v , and k_v to minimize the error. The parameter values for the best-fit naïve transfer function were $g_v = 0.48$, $\tau_v = 10.4$ s, and $k_v = 0.23$ (Fig. 3A and B).

The frequency response of the naïve goldfish VOR is described well as an HPF, with an order of about 0.2.

Previously, habituation has been modeled as a decrease in the time constant of the VOR HPF (see Introduction and Discussion). This operation decreases gain and increases phase lead (up to an asymptote) for all frequencies below the new corner frequency. This is illustrated for prototypical, order-1 HPFs in Fig. 1A and B, where the time constant of a naïve VOR HPF (dotted lines) is reduced by an order of magnitude (dot-dash lines). We examined the VOR frequency responses following habituation at specific, single frequencies. We find frequency-specific changes that cannot be explained as a decrease in the time constant of the naïve VOR HPF.

From the standpoint of systems analysis, it would be of interest to explore VOR frequency response characteristics at frequencies below 0.01 Hz in goldfish habituated at that frequency. Unfortunately, rapid habituation combined with long cycle periods at frequencies below 0.01 Hz mitigate against accurate estimation of gain and phase at those frequencies. Fortunately, a clear picture emerges from studies of VOR frequency-response characteristics in goldfish habituated at single frequencies that are higher than 0.01 Hz. Following 1 h of rotation at 0.03, 0.05, and 0.1 Hz, we observe a dip in gain at the habituating frequency and an increase and decrease in phase lead at frequencies above and below the habituating frequency, respectively (Fig. 3). The HPF model, which affects a broad range of frequencies, is inadequate to account for these frequency-specific effects. We suggest a more frequency-specific model for VOR habituation.

The most common linear dynamic element with frequency-restricted effects is the band-pass filter (BPF). A BPF can be constructed by combining a low- and a high-pass filter in series,

$$\frac{\dot{E}(s)}{\dot{H}(s)} = g_b \left(\frac{1}{s\tau_l + 1} \cdot \frac{s\tau_h}{s\tau_h + 1} \right)^{k_b}, \quad (5)$$

where g_b and k_b are the gain constant and order of the BPF, respectively. Time constants for the low (τ_l) and high (τ_h) pass filters define the low- and high-pass corner frequencies for the BPF (2). With the high-pass corner frequency less than the low-pass corner frequency (that is, $\tau_h > \tau_l$) the corner frequencies specify the pass band of the BPF. With the corner frequencies sufficiently far apart, the BPF has gain 1 and phase 0 for signals at frequencies within its pass band. But gain falls, and phase lead and lag increase to asymptotic values, as signal frequency respectively decreases and

increases outside of the pass band. The parameter k_b specifies the order of both the low- and the high-pass filters that compose the BPF. The phase asymptotes are ± 90 deg for an order-1 ($k_b = 1$) BPF.

For more tightly frequency-restricted BPFs it is useful to define a central frequency, which is equidistant between the two corner frequencies on a log scale. Because gain is falling off smoothly at the corner frequencies of the low- and high-pass filters that make up the BPF, the two corner frequencies can be brought close enough together that the BPF has a gain maximum at the center frequency, with gain falling off for all lower and higher frequencies. In this case gain at the center frequency can be less than 1. The phase characteristic, with order-1 low- and high-pass filters making up the BPF [$k_b = 1$ in (5)], passes from $+90$ deg to -90 deg as frequency increases, and has phase 0 at the center frequency. The frequency response of this type of BPF is illustrated in Fig. 1C and D.

To simulate a gain dip and phase crossover at the habituating frequency, the output of a tightly restricted BPF with central frequency equal to the habituating frequency could be subtracted from the output of the HPF model of the naïve VOR. This arrangement is schematized in Fig. 5, in which the outputs of a HPF and a BPF receiving the same input are differenced:

$$\frac{\dot{E}(s)}{\dot{H}(s)} = \text{HPF}(s) - \text{BPF}(s). \quad (6)$$

In this simplified model of the VOR, the input represents head rotational velocity (\dot{H}) and the output

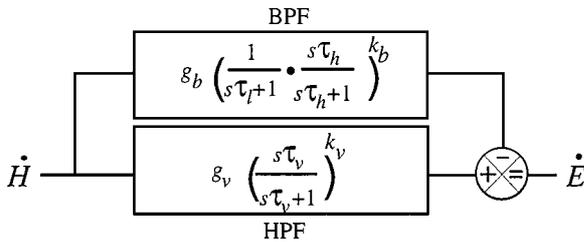


Figure 5. Schematic diagram of the combined HPF-BPF VOR model. The model converts head velocity (\dot{H}) to eye velocity (\dot{E}). The values used for the naïve goldfish HPF were: $\tau_v = 10.4$ s and $k_v = 0.23$. The gain constant of the HPF (g_v) was adjusted to match the highest gain value in the habituated data. The gain constant for the BPF (g_b) was fixed at 0.3 and the order (k_b) was fixed at 1.0. The time constants for the low- (τ_l) and high- (τ_h) pass filters that defined the BPF were determined separately for each frequency of habituation (see Results) using a least-squares optimization routine and are shown in Table 1.

represents the rotational velocity of the counterbalancing eye rotations (\dot{E}) produced by the VOR. The frequency-response characteristics of this model are shown in Fig. 1E and F as solid lines. The frequency-response characteristics of the naïve VOR HPF model are shown as dotted lines in Fig. 1E and F for comparison.

The VOR model schematized in Fig. 5 consists of a BPF and a HPF that receive the same head velocity (\dot{H}) input and compute eye velocity (\dot{E}) as the difference of their outputs. Subtraction of the BPF output would produce a dip in the gain characteristic of the model centered on the center frequency of the BPF. Since the HPF and BPF are in parallel, the BPF affects the phase of the frequency response of the HPF-BPF model in proportion to its gain at each frequency. Because the BPF output is subtracted, its contribution to phase is the inverse of the BPF phase shown in Fig. 1D. Thus, the inverted BPF phase goes from lead to lag as frequency decreases and remains zero at the center frequency. Adding this inverted phase to the HPF produces a phase crossover with increased and decreased lead for nearby frequencies above and below the center frequency, respectively.

We used an optimization routine to fit the HPF-BPF model (Fig. 5) to the data on frequency specific VOR habituation (Fig. 3). The optimization routine minimized the least-squares error (4) between the HPF-BPF model (6) and the data. To reduce the degrees of freedom allowed our model, we did not modify the parameter values generated by the least-squares fit of the HPF to the naïve data. However, to reduce the variability between each group of goldfish, the gain of the naïve VOR HPF (g_v) was set to match the peak median gain for each group. Only two parameters of the HPF-BPF model were iterated by the optimization routine, and both described the BPF: center frequency (cf in Hz) and λ . The log of the cf is equidistant between the logs of the corner frequencies of the low- and high-pass filters that make up the BPF. The parameter λ determined the separation in log units of the low- and high-pass corner frequencies from the center frequency. The following equations were used to calculate the low- and high-pass time constants in sec:

$$\tau_l = \frac{1}{cf \cdot 10^\lambda \cdot 2\pi} \quad (7a)$$

$$\tau_h = \frac{1}{cf \cdot 10^{-\lambda} \cdot 2\pi}. \quad (7b)$$

Table 1. Best-fit parameters of the BPF component of the HPF-BPF model. The habituating and center frequencies are both shown. λ is the distance in log units between the center frequency and the high- and low-pass corner frequencies. τ_h and τ_l are the time constants of the high- and low-pass filters, respectively (see (7)). g_v is the gain of the naïve VOR HPF, which was initially adjusted and then fixed (see text).

Habituating Frequencies (Hz)	cf (Hz)	λ	τ_l (s)	τ_h (s)	g_v
0.01	0.010	0.100	12.23	19.38	0.48
0.03	0.029	0.010	4.318	6.837	0.61
0.05	0.075	0.095	1.709	2.649	0.67
0.1	0.110	0.095	1.669	1.804	0.50

Varying cf and λ produced better convergence than varying τ_l and τ_h . Possible additional free parameters were the gain constant (g_b) and order (k_b) of the BPF ((5) and Fig. 5). The gain constant parameter was in some sense redundant because gain for tightly frequency restricted BPFs can also be manipulated by changing λ . The data were fit with the gain constant and order of the BPF fixed at 0.3 and 1, respectively. Allowing the least-squares minimization routine to iterate on the gain constant and order parameters did not appreciably improve the fit to the data.

A few data points were not included in the least-squares fit. These points were the 0.01 and 0.03 Hz gain points for goldfish that were habituated to 0.01 Hz, and the 0.03 Hz gain point for goldfish habituated at that frequency. Extremely low gain values of these points may have been the result of several nonlinear and non-stationary effects that selectively reduced gain during rotations at low frequencies (see Discussion).

Table 1 shows the best-fit values of the iterated free parameters cf and λ . Table 1 also reports the values of τ_l and τ_h , that are computed from cf and λ (7), and the value of naïve VOR gain (g_v) that was adjusted and then fixed for each case as explained above. The parameters g_v , k_v , τ_v , cf , λ , g_b , and k_b together specify the best-fit curves shown in Fig. 3. These best-fit curves provide a good qualitative fit to the data.

Discussion

The main finding of this study is that VOR habituation is not a generalized suppression of the response as previously supposed but is quite frequency specific. Previous assumptions were based on the view that habituation could be understood as a decrease in the time

constant (that is, increase in the corner frequency) of the HPF model of the VOR. Our findings argue against this view. We propose that a better, more frequency-specific linear approximation to habituated VOR dynamics can be obtained using a model in which the output of a BPF, with center frequency equal to the habituating frequency, is subtracted from the output of the HPF model of the VOR. We hypothesize that the BPF resides, in part, in the vestibulocerebellum. Our results and hypotheses are discussed further below.

Experimental

As in other animals, habituation of the goldfish VOR to sinusoidal rotation occurs only at lower frequencies (≤ 0.1 Hz) (Dow and Anastasio, 1997). Rotation for 1 h at higher frequencies (≥ 0.3 Hz) produced no statistically significant changes in either gain or phase. A decrease in gain at lower frequencies ($< \sim 0.15$ Hz), but no decrease in gain at higher frequencies, following 1 h of rotation at single frequencies has been reported previously in other animals (Ito et al., 1974; Kleinschmidt and Collewijn, 1975; Jäger and Henn, 1981a). However, effects on the overall frequency response have not been reported in these studies. Other similarities and differences in comparing VOR habituation in goldfish with VOR habituation and adaptation in the other animals are notable.

An interesting difference between our results and previous results concerns the time course of phase changes during habituation. Jäger and Henn (1981b) show how VOR phase lead evolves in one naïve human subject rotated continuously at 0.01 Hz. Phase lead gradually increased at that frequency from a naïve value of 45 deg to a plateau at around 60 deg after 60 to 80 min of continuous rotation. What happens with further rotation in human at 0.01 Hz has not been reported. Continued rotation at 0.01 Hz in goldfish shows that phase lead increases first but then decreases back toward naïve levels after reaching a peak (Fig. 4). Phase lead after 1 h of continuous rotation is not statistically different from the naïve phase lead at this frequency ($p > 0.05$).

Researchers have reported an increase in phase lead that occurs during habituation at low frequency in some primate studies (Jäger and Henn, 1981a, 1981b; Baloh et al., 1982) but not in others (Buettner et al., 1981; Jäger and Henn, 1981a). Since VOR plasticity is greater in goldfish than in other animals (Schaerer and Bennett, 1986; Pastor et al., 1992; Ratnam and

Anastasio, 1995; Weissenstein et al., 1996), it is possible that VOR habituation in goldfish represents an extreme form of this process. Changes in VOR due to habituation that are equivocal in other animals, like changes in phase, may be similar to those that are exhibited clearly in goldfish. The lack of a statistically significant change in phase lead at 0.01 Hz after 1 h of rotation at that frequency, in addition to the other frequency specific results, necessitates a change in the approach to modeling the effect of habituation on the VOR.

Systems Analysis

Previously, the frequency response of the habituated VOR had been modeled simply by decreasing the time constant of the HPF transfer function fit to the naïve VOR response (Blair and Gavin, 1979; Buettner et al., 1981; Jäger and Henn, 1981a; Baloh et al., 1982). The frequency response of the naïve VOR is approximated well by a HPF (Fig. 3A and B). A HPF with a shortened time constant was used as a simple and parsimonious model of VOR habituation. However, as shown above, the HPF is deficient as a model of the gold fish VOR following habituation at single frequencies. We propose the HPF-BPF as a better model (see below and Results).

Both the HPF and the HPF-BPF models are linear and stationary (that is, time invariant). Habituation in the goldfish is associated with nonlinear and nonstationary VOR behavior. We define nonlinearity and nonstationarity as, respectively, time-invariant and time-variant departures from a linear relationship between the input to (\dot{H}) and the output from (E) the VOR. Therefore, the best either the HPF or the HPF-BPF models can do is to describe a linear, stationary approximation to the habituated VOR. This approximation is made by identifying and removing from VOR data any nonlinear and nonstationary effects.

Nonstationarity in the habituated VOR is manifested most dramatically using a superposition paradigm. Under natural circumstances, the VOR is exposed to a superposition of a spectrum of frequencies of head rotation (Grossman et al., 1988). In a recent study (Dow and Anastasio, 1996), VOR gain in goldfish habituated at 0.01 Hz was found to increase almost to naïve levels (an increase of over 20 times) when the 0.01 Hz rotation was combined with a higher-frequency rotation. Gain immediately decreased again when the higher-frequency rotation was removed, showing that

the higher-frequency stimulus did not produce a permanent dishabituation. Rather, it appeared that the higher-frequency rotation caused VOR gain to switch abruptly from a low, habituated level to a higher level. Despite these very large changes in gain, changes in VOR phase at 0.01 Hz when combined with a higher-frequency rotation were variable and small.

The superposition results indicate that there is a component of habituation that can decrease VOR gain when presented with rotation at a low, habituated frequency and abruptly increase it again when presented with a rotation sufficiently different from the one to which it had been habituated. They further indicate that these abrupt changes in VOR gain can occur without appreciably affecting VOR phase. A similar mechanism appears to be at work under the present experimental circumstances. The gain of the VOR at the lowest frequencies (0.01 and 0.03 Hz), following habituation at those frequencies, is reduced to levels far lower than expected on the basis of phase measurements at those frequencies (see Results). We believe this is due to nonstationary decreases in VOR gain that minimally affect phase and that can occur at and near habituated frequencies but not at other frequencies. This nonstationarity could be simulated easily using the HPF-BPF model by decreasing the gain constant of the HPF component (parameter g_v in (3)) for frequencies at and near the habituated frequency but not at other frequencies. This was not done, however, because the goal was to find a descriptor of the habituated VOR that is better than the HPF, yet still linear and with parameters that are time-invariant. Therefore, rather than choose a different gain constant (g_v) value for each frequency, we simply excluded from the fits those gain values that were most severely affected by the nonstationarity. These were gains at 0.01 and 0.03 Hz for goldfish habituated at 0.01 Hz and gain at 0.03 Hz for goldfish habituated at that frequency (see Results). No phase values were excluded from any of the fits.

Another recent study explored the effects of nonstationarities and nonlinearities on the waveform of the habituating VOR (Dow and Anastasio, 1998a). It detailed abrupt reductions in gain occurring in the space of a few seconds and static distortions such as rectification of the VOR waveform. A bilateral neural network model was used to show that these static, nonlinear distortions could result if VOR suppression during habituation is brought about by inhibition of VN neurons that drives them into cut-off. These sorts of nonstationarities and nonlinearities are apparent in

the habituating VOR waveform shown in Fig. 2B. Distorted parts of the waveform, when they occurred, were excluded before the VOR responses were linearized by fitting sinusoids, for the purposes of estimating gain and phase at each single frequency (see Methods and Results).

Previous work characterized the nonstationarities and nonlinearities associated with VOR habituation (Dow and Anastasio, 1996, 1997, 1998a, 1998b). In the present analysis, the habituated VOR responses could be made approximately stationary and linear by identifying nonstationary and nonlinear aspects of the data and excluding them from the analysis. The approximately stationary and linear data can then be analyzed and modeled using the techniques of time-invariant, linear control systems theory (Milsom, 1966). This approach has a long tradition in vestibular and VOR neurophysiology (see Wilson and Melvill Jones, 1985 for a review).

The VOR has been described approximately using the HPF model, and VOR habituation has been modeled by shortening the time constant of the HPF (Blair and Gavin, 1979; Buettner et al., 1981; Jäger and Henn, 1981a; Baloh et al., 1982). Buettner and colleagues (1981) used a second-order HPF (with two distinct time constants) to fit VOR gain and phase data from monkeys that had been habituated to various low frequencies of rotation. A second-order HPF was necessary to match the low-frequency decrease in gain. However, even though the reported phase lead values for habituated monkey were greater at nearly all frequencies than naïve monkey, phases at the lowest frequency tested in habituated and naïve animals (0.0025 Hz) were nearly identical. The HPF filter model predicted that phase lead is still increasing at 0.0025 Hz rather than essentially the same value as the next highest frequency measured. Therefore, a HPF also appears to be inadequate to describe the habituated monkey VOR.

As shown above (see Results) the simple HPF is also deficient as a model of the habituated goldfish VOR even after the nonstationary and nonlinear aspects of the response are excluded from the analysis. The rather broadly extending effects of the HPF are inconsistent with the frequency-specific gain dip and phase crossover we observe in the VOR frequency response following habituation at single frequencies. The simplest time-invariant, linear model we found that can approximate the habituated VOR findings consists of one in which the output of a BPF, with center frequency equal (or nearly equal) to the habituating frequency,

is subtracted from the HPF model of the naïve VOR (Fig. 5; see Results).

The parameters of the HPF-BPF used to model our data are shown in Table 1. It is possible to decrease the gain of the BPF by decreasing λ (see Results). However, no trends were observed, suggesting that the variation in λ was a result of individual variation in the habituation of each goldfish and was not necessarily related to the frequency of habituation. The *cf* of the BPF matched the frequency of habituation in three of four cases. It differed only for 0.05 Hz, where the center frequency was 0.075 Hz. Examination of the phase data (Fig. 3H) shows that the phase points for 0.05 and 0.1 Hz straddle the naïve fit. This results in the phase crossover at a slightly higher frequency than the habituation frequency.

The HPF-BPF model also provides a possible explanation for simultaneous decrease in gain and the consistent rise and subsequent fall of phase lead observed during habituation to 0.01 Hz rotation (Fig. 4). Goldfish often start habituating during the first cycle of rotation at 0.01 Hz, presumably before a good estimate of the rotational frequency can be made. The data at 0.01 Hz (Fig. 4) are consistent with a BPF that starts out with a *cf* lower than the habituating frequency and gradually approaches the habituation frequency. The HPF-BPF model with a lower *cf* would produce a smaller gain decrease and would impart a phase lead at the habituating frequency. Bringing the *cf* closer to the habituating frequency would decrease gain further and would also bring phase back to the naïve level. An overshoot of *cf* could produce a phase lag at the habituating frequency. At higher habituating frequencies, a consistent relationship between decreasing VOR gain and phase changes during the process of habituation was not observed. More cycles occur at higher frequencies in the same amount of time, yet it takes longer for habituation to occur. Thus, at higher frequencies (≥ 0.03 Hz), more input concerning the rotational stimulus is available to the habituating process, allowing a better initial estimate of the *cf* for the BPF with less searching for the ideal *cf*. This would produce a decrease in gain with more variable changes in phase near the phase crossover.

Neurobiological Considerations

The HPF-BPF model ((6) and Fig. 5) was able to qualitatively reproduce the linear, stationary aspects of frequency-specific habituation in goldfish. This model

is neurobiologically plausible. The dynamics of the naïve VOR are well described using the HPF model (see Introduction and Results). Frequency-specific habituation in the goldfish can be modeled by including a BPF that receives the same input as the HPF and subtracts its output from that of the HPF. We hypothesize that the BPF resides, in part, in the vestibulocerebellum.

The VOR is mediated by brainstem VN neurons that receive head rotational velocity information from vestibular sensory neurons and send eye rotation commands to the eye muscle motoneurons. It is this basic three-neuron reflex that is modeled well as a HPF. The vestibulocerebellum also receives head-velocity information from the vestibular afferents (Llinás and Walton, 1990), so it receives essentially the same input as VN neurons. Also, Purkinje fibers from the vestibulocerebellum are inhibitory to VN neurons (Dow, 1936, 1938; Pastor et al., 1994; Butler and Hodos, 1996). Thus, the HPF-BPF model, with the HPF representing brainstem VOR pathways and the BPF primarily representing the vestibulocerebellum, is entirely consistent with known neuroanatomy.

Although there is no direct evidence that vestibulocerebellar Purkinje cells carry signals with BPF dynamics, we feel that the vestibulocerebellum would be a logical place to look for such signals. Previous models suggested that BPFs underlying frequency-specific adaptation were located in the brainstem (Lisberger et al., 1983; Miles et al., 1985), but these models are unrealistic neurophysiologically. The vestibulocerebellum is essential for VOR habituation in goldfish. Previous studies in our lab have shown the vestibulocerebellum to be necessary to produce and maintain habituation in goldfish (Dow and Anastasio, 1996, 1998a). The vestibulocerebellum also receives input from vestibular nucleus neurons (Llinás and Walton, 1990). Thus, the most parsimonious hypothesis is that the BPF mediating frequency-specific VOR habituation resides jointly in the brainstem and the vestibulocerebellum, with the integrity of the latter being essential.

Frequency-specific effects, including the gain dip and phase crossover, are observed when VOR gain is reduced at single frequencies in vestibular/visual adaptation experiments (Godaux et al., 1983; Lisberger et al., 1983; Schairer and Bennett, 1986; Raymond and Lisberger, 1996). The VOR frequency responses following single-frequency down adaptation or following single-frequency habituation are strikingly similar. This is especially so for the phase characteristics.

The only apparent difference is that the nonstationary reduction in VOR gain, which reduces gain at low frequencies far more than expected based on phase measurements at those frequencies (see above), does not appear to be at work in the down-adapted VOR. It may be the case in general that nonlinear and nonstationary VOR behavior is correlated more with habituation than with adaptation.

In mammals, different areas of the vestibulocerebellum are necessary for VOR adaptation and habituation. The flocculus is necessary for vestibular adaptation (Robinson, 1976; Zee et al., 1981; Waespe et al., 1983; Lisberger et al., 1984; Torte et al., 1994), while the nodulus and uvula are necessary for vestibular habituation (Singleton, 1967; Waespe et al., 1985; Cohen et al., 1992; Torte et al., 1994). Though the goldfish cerebellum does not have distinct lobules, a vestibulocerebellum has been identified (Pastor et al., 1994). The goldfish vestibulocerebellum is necessary both for complete VOR adaptation to occur (Pastor et al., 1994) and for habituation to occur and be maintained (Dow and Anastasio, 1996, 1998a).

For the goldfish VOR, both adaptation (Schairer and Bennett, 1986) and habituation (this study) are frequency-specific. It is impossible to know at the present time whether adaptation and habituation are mediated by different parts or the same part of the goldfish vestibulocerebellum. The cerebellum is highly conserved for different species and has little variability with regard to its neural elements (Llinás and Walton, 1990). Therefore, it is not unreasonable to suppose that different cerebellar regions are equally capable of producing frequency-specific forms of VOR plasticity. It would be interesting to see if VOR habituation in mammals, which is known to be mediated by a part of the vestibulocerebellum different from that which mediates VOR adaptation, is also frequency-specific. In any case, frequency-specific habituation, described for the first time here in goldfish, has not been studied systematically in any other animal.

Conclusion

Habituation of the VOR has been explained previously as a decrease in the time constant of the high-pass filter model of the naïve (that is, not previously habituated) VOR. We have shown that habituation is frequency specific, in that gain decreases primarily at the frequency of habituation, and there is an increase and decrease in phase lead at nearby frequencies above

and below the habituating frequency, respectively. This frequency-specific gain dip and phase crossover that we observe in our data makes a pure high-pass filter model of VOR habituation inadequate. We show that the data are consistent with a model in which a band-pass filter and a high-pass filter receive the same input and difference their outputs. We hypothesize that the band-pass filter resides, in part, in the vestibulocerebellum because it receives the same input as, but is inhibitory to, the vestibular nuclei neurons that mediate the VOR. Our model qualitatively fits our data by producing a VOR gain dip and a phase crossover at the habituating frequency.

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